Message Text

UNCLASSIFIED

PAGE 01 STATE 056281

63
ORIGIN HEW-06

INFO OCT-01 EA-09 ISO-00 OES-05 /021 R

DRAFTED BY DHEW/FDA: JRWEINROTH, M.D.: AMS
APPROVED BY OES/APT/BMP: WJWALSH, III
DHEW/OIH: MACODDING
EA/ANP:MMICHAUD INFO
---------- 048376
O 082223Z MAR 76
FM SECSTATE WASHDC
TO AMEMBASSY CANBERRA IMMEDIATE

UNCLAS STATE 056281

E.O. 11652: N/A

TAGS: TBIO, AS

SUBJECT: REQUEST FOR INFORMATION ON ANTI-CANCER DRUG FROM AUSTRALIAN DEPARTMENT OF HEALTH

REF: CANBERRA 1120, 1402

1. FDA REGRETS DELAY IN REPLY TO CANBERRA 1120 WHICH WAS NOT RECEIVED IN THE OFFICE OF INTERNATIONAL AFFAIRS, FDA UNTIL ALERTED BY CANBERRA 1402 THAT IT EXISTED.

2. MARUYAMA VACCINE IS AN AQUEOUS EXTRACT OF POLY-SACCHARIDE AND NUCLEIC ACID MATERIALS FROM TUBERCLE BACILLI DERIVED FROM A HUMAN SOURCE. IT HAS SOME SIMILARITIES TO METHANOL EXTRACTED RESIDUE OF BACILLE CALMET-GUERIN VACCINE (MER-BCG) AS WELL AS TO BCG VACCINE, BOTH OF WHICH ARE CURRENTLY UNDERGOING INVESTIGATIONAL USE IN THE UNITED STATES FOR THE TREATMENT OF MALIGNANT DISEASE. THUS AT LEAST A THEORETICAL RATIONALE EXISTS THAT MARUYAMA VACCINE COULD POSSIBLY HAVE A BENEFICIAL EFFECT.

3. ALTHOUGH THERE WERE NO DATA FROM ANIMAL TUMOR STUDIES
UNCLASSIFIED

UNCLASSIFIED

PAGE 02 STATE 056281

TO INDICATE THE POSSIBLE EFFICACY OF THIS VACCINE,

THERE WAS SUFFICIENT SCIENTIFIC LITERATURE TO SUPPORT THE

RESTRICTED USE OF MARUYAMA VACCINE. PAPERS WERE PRESENTED TO THE XITH INTERNATIONAL CANCER CONGRESS, FLORENCE, ITALY, 20-26 OCT. 1974: "ON THE TREATMENT OF MALIGNANT TUMORS WITH AN EXTRACT FROM TUBERCLE BACILLI" BY CHISATO MARUYAMA, M.D., AND KEISHIRO FUGITA, M.D., AND "THE CLINICAL AND HISTOLOGIC ASSESSMENT OF THE THERAPEUTIC EFFECTS OF AN EXTRACT FROM TUBERCLE BACILLI (MARUYAMA VACCINE) ON CANCER" BY KEISHIRO FUGITA, M.D., MASAMICHI KOSEIKI, M.D., AND CHISATO MARUYAMA, M.D., DETAILING STUDIES INVOLVING 2,474 PATIENTS BETWEEN 1965 AND 1973. THE MONOGRAPH ENTITLED "ON THE TREATMENT OF MALIGNANT TUMORS WITH AN EXTRACT FROM TUBERCLE BACILLI WITH THE SUMMARY AND SOME ILLUSTRATIONS OF THE CLINICAL RESULTS IN 1965-1971" BY CHISATO MARUYAMA, M.D. WAS ALSO AVAILABLE FOR REVIEW.

4. ALTHOUGH IT IS TRUE THAT MARUYAMA VACCINE HAS BEEN USED ONLY IN UNCONTROLLED CLINICAL STUDIES IN THE UNITED STATES TO DATE, IT IS DIFFICULT TO SEE WHAT TYPE OF CONTROL SUBJECTS, OTHER THAN PLACEBO OR UNTREATED CONTROLS, COULD BE SELECTED FOR PATIENTS WITH TERMINAL MALIGNANT DISEASE FOR WHOM ALL FORMS OF CONVENTIONAL ACCEPTED THERAPY HAVE BEEN EXHAUSTED. A CLINICAL INVESTIGATOR WOULD BE IN A DIFFICULT POSITION, WHEN OBTAINING INFORMED CONSENT FROM SUCH A GROUP, TO CONVINCE HALF THE GROUP THAT THEY SHOULD RECEIVE EITHER NO TREATMENT OR A PLACEBO RATHER THAN AN EXPERIMENTAL

MYCOBACTERIAL ANTIGEN DRUG THAT MIGHT POSSIBLY BE OF BENEFIT TO THEM.

5. DR. MARUYAMA IS FORMER DIRECTOR OF THE NIPPON MEDICAL SCHOOL IN TOKYO AND IS REGARDED AS A REPUTABLE SCIENTIST. SINCE THIS VACCINE IS PRODUCED OUTSIDE THE UNITED STATES, OUR ABILITY TO OBTAIN CLINICAL RECORDS OR OTHER DETAILED INFORMATION REGARDING PATIENTS TREATED WITH THIS PRODUCT WAS LIMITED. ONE WAY OF OVERCOMING THIS LIMITATION AND OBTAINING IN THE SHORTEST POSSIBLE UNCLASSIFIED

TIME AN EVALUATION OF THESE FOREIGN CLINICAL DATA WAS TO ALLOW INDIVIDUAL AMERICAN PHYSICIANS TO FILE "RESTRICTED" INVESTIGATIONAL NEW DRUG (IND) APPLICATIONS THAT LIMIT THE NUMBER OF PATIENTS TREATED TO THOSE FOR WHOM ALL AVAILABLE FORMS OF ACCEPTED CANCER THERAPY HAVE BEEN UNSUCCESSFULLY EXHAUSTED. THESE PHYSICIANS HAVE BEEN REQUESTED TO SUBMIT FREQUENT REPORTS OF THEIR OBSERVATIONS OF THE SAFETY AND EFFICACY OF THIS VACCINE. RESPONSE TO

THESE REQUESTS HAVE BEEN BOTH PROMPT AND COOPERATIVE. TO DATE, FDA HAS BEEN UNABLE TO ELICIT ANY ADVERSE REACTIONS

ASSOCIATED WITH THE USE OF THIS DRUG. THROUGH INSISTING ON THE USE OF DETAILED AND SPECIFIC PATIENT CONSENT FORMS AND PROHIBITING ANY COMMERCIALIZATION OF MARUYAMA VACCINE IN THESE STUDIES, WE HAVE GUARDED AGAINST POSSIBLE EXPLOITATION OF THESE PATIENTS.

6. RESULTS TO DATE INDICATE THAT OF THE 130 IND APPLICATIONS APPROVED, THERE HAVE BEEN 95 REPLIES TO THE AFOREMENTIONED PHYSICIAN REPORTS. 23 ARE NOT EVALUABLE. OF THE 72 THAT ARE EVALUABLE, THE FOLLOWING DATA IS PERTINENT:

4 PATIENTS (5 PERCENT) WERE WORSE.
5 PATIENTS (7 PERCENT) HAD OBJECTIVE IMPROVEMENT.
38 PATIENTS (53 PERCENT) DEMONSTRATED NO SUBJECTIVE OR OBJECTIVE IMPROVEMENT.
25 PATIENTS (35 PERCENT) DEMONSTRATED OBJECTIVE IMPROVE-MENT ONLY.

7. IN MONITORING WHAT FDA CONSIDERS TO BE A VERY DIF-FICULT AREA, OUR BUREAU OF BIOLOGICS HAS MET WITH THE DIRECTOR AND DEPUTY DIRECTOR OF THE DIVISION OF CANCER BIOLOGY AND DIAGNOSIS, NCI (THAT DIVISION OF THE NATIONAL

CANCER INSTITUTE CONCERNED WITH IMMUNOTHERAPY FOR CANCER" TO INSURE THAT OUR HANDLING OF THIS MATTER IS CONSISTENT WITH THEIR BEST JUDGMENT. WE ARE KEEPING THEM CLOSELY INFORMED OF THE RESULTS REPORTED TO US UNDER THESE IND APPLICATIONS, AND WE PLAN TO MEET WITH THEM PERIODICALLY TO FURTHER EVALUATE OUR POSITION.
UNCLASSIFIED

UNCLASSIFIED

PAGE 04 STATE 056281

8. IT IS FDA'S INTENT IN THE IMMEDIATE FUTURE TO OBTAIN ADDITIONAL PERTINENT INFORMATION FROM DR. MARUYAMA, IN ORDER TO PERMIT ADEQUATE AND WELL-CONTROLLED CLINICAL STUDIES DEMONSTRATING THE SAFETY AND EFFICACY OF THIS PRODUCT UNDER THE USUAL TYPE OF IND FILING AND THEREFORE TO CEASE ACCEPTING NEW "RESTRICTED" IND FILINGS. IT HAS BEEN FDA'S INTENTION THROUGHOUT TO ACT COMPASSIONATELY FOR CANCER VICTIMS WHILE GIVING CAREFUL CONSIDERATION TO OUR SCIENTIFIC AND LEGAL RESPONSIBILITIES. KISSINGER

UNCLASSIFIED

NNN

Margaret P. Grafeld Declassified/Released US Department of State EO Systematic Review 04 MAY 2006

Message Attributes

Automatic Decaptioning: X
Capture Date: 01 JAN 1994
Channel Indicators: n/a
Current Classification: UNCLASSIFIED
Concepts: RESEARCH, CANCER, VACCINES, INTERGOVERNMENTAL COOPERATION
Control Number: n/a
Copy: SINGLE
Draft Date: 08 MAR 1976
Decaption Date: 01 JAN 1960
Decaption Note:
Disposition Action: n/a
Disposition Approved on Date:
Disposition Authority: n/a
Disposition Case Number: n/a
Disposition Comment:
Disposition Date: 01 JAN 1960
Disposition Event:
Disposition History: n/a
Disposition Reason:
Disposition Remarks:
Document Number: 1976STATE056281
Document Source: CORE
Document Unique ID: 00
Drafter: JRWEINROTH, M.D.: AMS
Enclosure: n/a
Executive Order: N/A
Errors: N/A
Film Number: D760087-1118
From: STATE
Handling Restrictions: n/a
Image Path:
ISecure: 1
Legacy Key: link1976/newtext/t19760383/aaaacvju.tel
Line Count: 164
Locator: TEXT ON-LINE, ON MICROFILM
Office: ORIGIN HEW
Original Classification: UNCLASSIFIED
Original Handling Restrictions: n/a
Original Previous Classification: n/a
Original Previous Handling Restrictions: n/a
Page Count: 3
Previous Channel Indicators: n/a
Previous Classification: n/a
Previous Handling Restrictions: n/a
Reference: 76 CANBERRA 1120
Review Action: RELEASED, APPROVED
Review Authority: ShawDG
Review Comment: n/a
Review Content Flags:
Review Date: 29 JUN 2004
Review Event:
Review Exemptions: n/a
Review History: RELEASED <29 JUN 2004 by fisherem>; APPROVED <14 DEC 2004 by ShawDG>
Review Markings:

Margaret P. Grafeld
Declassified/Released
US Department of State
EO Systematic Review
04 MAY 2006

Review Media Identifier:
Review Referrals: n/a
Review Release Date: n/a
Review Release Event: n/a
Review Transfer Date:
Review Withdrawn Fields: n/a
Secure: OPEN
Status: NATIVE
Subject: REQUEST FOR INFORMATION ON ANTI-CANCER DRUG FROM AUSTRALIAN DEPARTMENT OF HEALTH
TAGS: TBIO, AS, US
To: CANBERRA
Type: TE
Markings: Margaret P. Grafeld Declassified/Released US Department of State EO Systematic Review 04 MAY 2006